Trends in Prostate Cancer Incidence and Mortality in New Mexico Are Consistent with an Increase in Effective Screening

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Abstract
The increasing occurrence of prostate cancer in the United States has led to recommendations for routine prostate cancer screening in men aged 50 years and older. Although present methods of prostate cancer screening have not been shown to reduce mortality, screening using digital rectal examination or prostate-specific antigen does detect tumors at earlier stages. To assess whether trends in incidence and mortality rates are consistent with an increase in effective screening in New Mexico, we examined prostate cancer incidence rates calculated from data collected by the New Mexico Tumor Registry for the years 1969–1991, and mortality rates calculated from data collected by the New Mexico Bureau of Vital Statistics for the years 1958–1991. Population-based measures of prostate cancer screening frequency in New Mexico are not available for the period of this study; however, the proportion of prostate cancers detected by screening, as documented by a review of records from a random sample of prostate cancer cases, increased 3-fold, from 13% during the 1969–1972 period to 41% in the 1988–1991 period. During the period of study, age-adjusted incidence rates increased from 66.3 to 122.3/100,000 men. Stage migration from distant to earlier stages was apparent in the increase in the proportion of early stage cancers from 77.5 to 85.5%, and the decrease of distant stage cancers from 21.2 to 9.8%. Stage-specific incidence rates increased for local (87.3%) and regional stage cancers (283.0%), and decreased for distant stage cancers (16.0%). Average annual age-adjusted mortality rates for prostate cancer decreased from 23.0/100,000 in the 1978–1982 period to 21.6/100,000 (6.1%) in the 1988–1991 period. Mortality peaked at 26.8/100,000 in 1980 and decreased to 21.2/100,000 by 1991. The decrease in mortality rates is consistent with stage migration from distant to earlier stages of disease and may reflect an increase in effective prostate cancer screening.

Introduction
Rates of prostate cancer incidence and mortality have been increasing in the United States since 1960 (1, 2). During the period 1973–1989, nationwide incidence rates increased from 64.1 to 109.3/100,000 men, a 3% average annual increase, and mortality rates increased from 21.7 to 25.5/100,000 (1). Because few modifiable etiological factors are known for prostate cancer, the public health response to the increasing rates has been directed primarily toward increased screening to detect prostate cancers at early, treatable stages of disease.

Although routine screening for prostate cancer has been recommended for many years by the American Cancer Society and the National Cancer Institute, no evidence has been reported that screening for prostate cancer reduces mortality (3–7). The effectiveness of prostate cancer screening is being studied as part of a randomized cancer screening study, the Prostate, Lung, Colon and Ovary trial, although the results of this study will not be available for at least a decade. In the interim, examination of trends in prostate cancer screening and disease occurrence may be useful in evaluating the effectiveness of screening methods and their performance as part of the existing medical care system (8). Although this approach may be subject to a number of biases, studies of the relationship between trends in screening and disease occurrence have produced useful results in the past (9). For example, studies of trends in incidence and mortality for cervical cancer following changes in screening have contributed to evaluation of the effectiveness of endocervical Papanicolaou smears, a screening method never tested in a randomized trial (1).

Because the effectiveness of prostate cancer screening is unknown, we studied the relationship between screening and temporal patterns of incidence and mortality for prostate cancer in New Mexico, where population-based cancer data have been collected by the New Mexico Tumor Registry (NMTR)3 since 1969. We compared average annual age-adjusted, age-specific, and stage-specific prostate cancer incidence rates and stage-specific relative 5-year survival from 1969 to 1991 with the age-adjusted and age-specific mortality rates from 1958 to 1991. To examine the role that increased screening efforts may have played in incidence

3 The abbreviations used are: NMTR, New Mexico Tumor Registry; SEER, Surveillance, Epidemiology, and End Results; ICD, International Classification of Diseases for Oncology; PSA, prostate-specific antigen; TURP, transurethral resection of the prostate; CI, confidence interval.
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and mortality patterns in the state, we investigated temporal changes in the proportion of cases detected by screening and changes in the stage distribution from 1973 to 1991. To evaluate the effect of length-time bias on survival, we examined temporal changes in the histological grade of prostate tumors from 1985 to 1991. In addition, we studied the effects of the increased use of radical prostatectomies on staging and survival.

Materials and Methods

The NMTR is a member of the SEER Program of the National Cancer Institute. The Registry has recorded population-based cancer incidence in New Mexico since 1969 (10). Cancer cases are identified through active surveillance of hospital records, outpatient clinic records, pathology and autopsy reports, and radiation therapy records. The registry staff also reviews state death certificates that mention cancer. We obtained ICD-coded death certificate data for the period 1958–1991 from the New Mexico Bureau of Vital Statistics. Prostate cancer deaths were coded as 177–177.9 in the seventh ICD revision (1958–1968) and 185–185.9 in the eighth and ninth ICD revisions (1969–1978 and 1979–1991, respectively). Histological grade was assigned using ICD-O Edition 2 categories (11).

Stage of disease was classified using the SEER definitions for extent of disease and summary stages (12–14). Because changes in extent of disease coding occurred during the period of study, summary stages of local, regional, distant, and unknown were used. The analyses by stage do not include incidence rates for in situ cancers as only 20 cases were reported. Local cancers were defined as those confined to the prostate. Regional cancers were those that involved local structures and local lymph nodes, and distant cancers extended beyond periprostatic tissue and local nodes or were metastatic. Cancers were assigned to the unknown category if information was not sufficient to assign a stage or if staging occurred more than 2 months after histological diagnosis (14, 15). A change in coding for surgical intervention was implemented in 1988 (13). Men who did not have surgery or underwent needle biopsy only, and had no evidence for metastases, were classified as unknown stage starting in 1988. Previously, these cases were classified primarily as local or regional stage disease. All cases with unknown stage were reviewed by the staff and additional staging information was obtained when possible.


We employed the direct method to calculate age-adjusted rates using the 1970 United States population as a standard. CIs were calculated assuming that rates followed a Poisson distribution (24). Relative 5-year survival was calculated using the method described by Ederer et al. (25). The 1980 lifetable for United States white males was used in the relative survival calculations. Analyses were performed using the SAS statistical analysis system (26) and PC DaSH (27).

Changes in prostate cancer screening in New Mexico were estimated using several data sources. Although the NMTR does not routinely analyze the presenting signs and symptoms at diagnosis or the number of screening-detected cases, information concerning the reasons or the physician visit that lead to the diagnosis of prostate cancer has been collected. To determine the proportion of prostate cancer cases detected by screening, a special review was made of a random sample of NMTR prostate cancer cases, stratified in 5-year periods. The reasons for presentation included routine physical examination, screening programs, voiding symptoms, urinary obstruction, pain, and other signs and symptoms. To further estimate the effect of screening, we examined data on the number of PSA assays performed by major reference laboratories in the Albuquerque metropolitan area and on the number of men screened during Prostate Cancer Awareness Week, the major statewide screening effort. Changes in the proportion of local and regional stage prostate cancers treated by radical prostatectomy were documented using treatment data collected by the NMTR. Changes in stage from preoperative to postoperative classification were evaluated using a standard review of medical records for prostate cancer patients. All patients who underwent radical prostatectomy at two major referral institutions in Albuquerque in the period 1983–1991 were identified using NMTR data; pre- and postoperative stages were abstracted from their hospital medical records.

Results

From 1969 to 1991, 10,387 cases of prostate cancer were reported in New Mexico. Of these cases, 95% were confirmed histologically; the remaining 5% were diagnosed by clinical exam, radiological procedures, and unknown methods, or were cases ascertained from death certificates. The reasons for patient presentation that led to the diagnosis of prostate cancer changed from 1973 to 1991, the time period for which data were available. More cases were diagnosed by routine examinations and screening programs. The proportion of cases detected by screening increased 3-fold from 13.0–41.2% (Table 1). Before 1990, the majority of screening-detected cases were diagnosed using digital rectal

<table>
<thead>
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<th>Years</th>
<th>Screening</th>
<th>Voids</th>
<th>Obstruction</th>
<th>Pain</th>
<th>Autopsy</th>
<th>Other</th>
<th>Unknown</th>
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<tbody>
<tr>
<td></td>
<td>% No.</td>
<td>% No.</td>
<td>% No.</td>
<td>% No.</td>
<td>% No.</td>
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<td>% No.</td>
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<td>1973-77</td>
<td>13.0 (16)</td>
<td>8.1 (10)</td>
<td>38.2 (47)</td>
<td>15.5 (19)</td>
<td>2.4 (3)</td>
<td>15.5 (19)</td>
<td>7.3 (9)</td>
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<tr>
<td>1978-82</td>
<td>11.0 (14)</td>
<td>18.9 (24)</td>
<td>43.4 (55)</td>
<td>9.4 (12)</td>
<td>1.6 (2)</td>
<td>10.2 (13)</td>
<td>1.6 (2)</td>
</tr>
<tr>
<td>1983-87</td>
<td>22.0 (39)</td>
<td>35.1 (62)</td>
<td>7.9 (14)</td>
<td>4.5 (8)</td>
<td>1.1 (2)</td>
<td>10.2 (18)</td>
<td>18.2 (34)</td>
</tr>
<tr>
<td>1988-91</td>
<td>41.2 (63)</td>
<td>29.4 (45)</td>
<td>9.8 (15)</td>
<td>0.0 (0)</td>
<td>0.0 (0)</td>
<td>1.8 (17)</td>
<td>8.5 (13)</td>
</tr>
</tbody>
</table>
examination. No cases in the random sample were diagnosed using PSA; however, in the period 1990–1991, PSA was used to diagnose 7.2% of cases. In addition to the increase in screening-detected cases, the severity of presenting signs and symptoms decreased. From 1973 to 1991, the proportion of cases diagnosed as a result of marked obstruction, retention, and pain decreased, and the proportion diagnosed as a result of milder voiding symptoms, such as nocturia and hesitancy, increased.

A stage migration from distant stage cancers at diagnosis to earlier stage lesions occurred over the 23-year study period (Table 2). Although the proportion of local stage cancers did not change substantially from 1969 to 1991, the proportion of disease diagnosed at a local or regional stage increased from 77.5% in the 1969–1972 period to 85.4% in the 1988–1991 period. Regional stage disease increased from 6.4% to 13.2% of all diagnosed prostate cancers, while distant stage disease fell from 21.7% to 9.8%. Cases with unknown stage cancers increased from 0.9% to 4.7% over the period of study.

From 1969 to 1991, age-adjusted incidence rates for all stages of prostate cancer diagnosed in New Mexico rose from 66.3 to 122.3/100,000 (84.5%), a 3% average annual rate of change (Table 3). The rise in incidence rates reflected a marked rise in incidence of early stage disease. Local stage incidence rates increased from 47.1 to 88.2/100,000 (87.3%). The incidence rates for regional stage prostate cancer increased from 4.2 to 16.1/100,000 (283%). In contrast, the age-adjusted incidence for distant-stage disease at diagnosis decreased from 14.4 to 12.1/100,000 (16.7%). The age-adjusted incidence for cancers of unknown stage increased from 0.5% to 5.8/100,000 over the same period.

Age-specific incidence rates for prostate cancer increased for all age groups in successive birth cohorts (Fig. 1). Increases were greatest in the 65 to 69- and 70 to 74-year age groups. The changes in age-specific incidence rates reflected the increased incidence rates for early stages of disease at diagnosis (data not shown). Age-specific incidence rates increased in successive birth cohorts starting in the same calendar period, which suggests that a change occurred during the same time period among all birth cohorts.

The 5-year relative survival for local and regional stage disease increased for each age group over the period from 1969 to 1987 (Table 4). The increase in survival was greatest for early stage cases 70 years and older. For distant stage disease, 5-year relative survival did not vary substantially by age or period. During the 1978–1982 and 1983–1987 periods, relative 5-year survival was lower among men diagnosed at less than 60 years and those diagnosed at 75 years and older compared with men aged 60–69 and 70–74 years.

Treatment for local and regional stage prostate cancer changed over the period of study. Radical prostatectomy was used to treat an increasing proportion of early stage cancers (Table 5). From 1983 to 1991, the proportion of local and regional cases treated with radical prostatectomy increased from 10.3% to 34.7%. The increased use of radical prostatectomy produced more accurate staging information compared with other diagnostic and treatment modalities. The increased accuracy resulted in the reclassification of the majority of early stage cancers to more advanced stages postoperatively (Table 6).

To investigate whether recently diagnosed cancers were less aggressive than those diagnosed previously, we studied changes in histological grade from 1985 to 1991, the period for which detailed histological grade data are available. Well differentiated cancers decreased in proportion from 30.7% in 1985 to 27.5% in 1991, and moderately differentiated cancers increased from 33.9% to 44.8% over the same period (Fig. 2). The proportion of poorly differentiated, undifferentiated, and unclassified tumors changed little. The trends for histological grade continued into 1992.

Age-adjusted mortality rates among New Mexicans increased from 15.7/100,000 in the 1958–1962 period to a peak of 23.0/100,000 in the 1977–1982 period. By the 1988–1991 period, mortality rates decreased 6.1%, to 21.6/100,000 (Table 7). Mortality rates for prostate cancer peaked in 1980 at 26.8/100,000 (95% CI, 22.1–31.6) and decreased to 21.2/100,000 (95% CI, 17.8–24.6) in 1991. Mortality rates appear to have decreased slightly in later birth cohorts among the 55 to 59-, 60 to 64-, 65 to 69-, and 70 to 74-year age groups (Fig. 3). Among men aged 75 years and older, prostate cancer mortality rates increased approximately 50% for successive birth cohorts through 1983 and then reached a plateau.

Discussion

The pattern of increasing incidence of early stage tumors and decreasing incidence of distant stage tumors suggests that earlier detection of prostate cancers contributed to the reduction in mortality rates after 1980. The stage migration is consistent with that expected from increased screening for prostate cancer. Population-based measures of prostate cancer screening in New Mexico are not available for the period of study; however, the 3-fold increase in screening-detected cases in our review of NMTR records suggests that increased screening efforts among New Mexican men have occurred. From 1969 to 1991, digital rectal examination was the primary screening modality used to detect prostate cancers. The shift in stage of disease at diagnosis is consistent with that expected from increased prostate cancer screening using digital rectal examination (7, 28–30). Other data also indicate an increase in the frequency of screening in New Mexico during the 1980s. In 1989, statewide prostate cancer screening programs began as part of the nationwide Prostate Cancer Awareness Week (28). In the 1989–1991 period,
3100 men were screened during Prostate Cancer Awareness Week in New Mexico. More than 48 cases of prostate cancer were diagnosed, representing 7% of total cases reported for the period. In addition to the increase in screening-detected cases using digital rectal examination, the use of PSA for screening increased, as indicated by the rise of cancers detected by PSA during the 1988-1991 period and the 20-fold increase in the number of PSA tests conducted in three major clinical laboratories in the Albuquerque metropolitan area from 1985 to 1991. Although the use of PSA for screening may increase the detection of early stage cancer (31, 32), widespread use of PSA has been too recent to affect mortality rates substantially.

Over the period of study, the increase in cancers detected by screening was paralleled by a stage shift from distant to regional stage disease at diagnosis; however, the expected increase in the proportion of cancers diagnosed at a local stage did not occur. The lack of increase may have resulted from the performance characteristics of digital rectal examination or the high frequency of postoperative stage reclassification following radical prostatectomy. The prostate cancers detected by digital rectal examination are often diagnosed at a regional or distant stage, and 42-58% of those initially classified as localized are upstaged postoperatively (30, 33-37). The increased use of radical prostatectomy in the treatment of prostate cancer is likely to have upstaged a greater proportion of localized tumors into the regional stage category.

Although the performance of digital rectal examination in detecting localized disease may not be optimal, a reduction in distant stage tumors may be more important in producing a decrease in mortality. Because localized prostate

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**Table 3** Prostate cancer age-adjusted incidence for local, regional, and distant stage at diagnosis in New Mexico men, 1969-1991

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<tbody>
<tr>
<td></td>
<td>Rate</td>
<td>95% CI</td>
<td>Rate</td>
<td>95% CI</td>
<td>Rate</td>
</tr>
<tr>
<td>Local</td>
<td>47.1</td>
<td>(43.5-50.7)</td>
<td>47.5</td>
<td>(44.5-50.5)</td>
<td>60.7</td>
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<tr>
<td>Regional</td>
<td>4.2</td>
<td>(3.1-5.3)</td>
<td>4.8</td>
<td>(3.8-5.8)</td>
<td>5.2</td>
</tr>
<tr>
<td>Distant</td>
<td>14.4</td>
<td>(12.4-16.4)</td>
<td>13.0</td>
<td>(11.4-14.6)</td>
<td>12.9</td>
</tr>
<tr>
<td>Unknown</td>
<td>0.5</td>
<td>(0.1-0.9)</td>
<td>0.9</td>
<td>(0.5-1.3)</td>
<td>2.0</td>
</tr>
<tr>
<td>All Stage</td>
<td>66.3</td>
<td>(62.0-70.6)</td>
<td>66.1</td>
<td>(62.5-69.7)</td>
<td>80.9</td>
</tr>
</tbody>
</table>

* Per 100,000 adjusted to the 1970 United States standard population.

**Table 4** Prostate cancer 5-year relative survival among New Mexico men, diagnosed 1969-1991

<table>
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<tr>
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<tbody>
<tr>
<td>Local</td>
<td>90.4</td>
<td>94.7</td>
<td>95.4</td>
<td>84.2</td>
</tr>
<tr>
<td>Regional</td>
<td>62.6</td>
<td>84.7</td>
<td>71.7</td>
<td>65.1</td>
</tr>
<tr>
<td>Distant</td>
<td>30.0</td>
<td>33.4</td>
<td>34.5</td>
<td>26.7</td>
</tr>
<tr>
<td>All</td>
<td>77.0</td>
<td>85.2</td>
<td>80.1</td>
<td>83.2</td>
</tr>
</tbody>
</table>

* Less than 10 cases from 1969-1972.
cancer has excellent survival at 5 and 15 years (38, 39), the
detection and treatment of localized disease is unlikely to
reduce mortality substantially. In contrast, distant stage pros-
tate cancer has a poor 5-year relative survival, and reduction
of distant stage disease by early detection is expected to
decrease mortality if treatment of earlier stage tumors is
effective.

The reasons for the contrasting trends for mortality in
New Mexico and the United States as a whole are uncertain.
Through 1987, SEER incidence rates for distant stage prostate
cancers did not decrease (24), a finding consistent with the
rising prostate cancer mortality up to that date. Differences in
screening are a possible explanation for the lack of stage
shift or decrease in mortality. Although direct measures of
national screening frequency are not available, indirect data
suggest that men residing in New Mexico may participate in
screening programs more actively than men nationwide, as
suggested by the higher per capita participation rate for the
Prostate Cancer Awareness Week in New Mexico than that
of other states. Differences in treatment, distribution of risk
factors for prostate cancer, and access to medical care in
New Mexico compared with the United States as a whole
also may have contributed to the contrasting trends (22, 23,
40, 41).

Although increased screening efforts are likely to un-
derlie the stage migration from distant stage to earlier stages
of disease at diagnosis, other factors, such as changes in surgical practices, presenting signs and symptoms for pa-
tients undergoing TURP, SEER program coding procedures,
and risk factors for prostate cancer also may have contrib-
ted to the changes in incidence. Changes in the proportion of
cases diagnosed as a result of TURP for severe symptoms, such as
severe obstruction, complete urinary retention, obstructive
urethropy, and pain decreased, and the proportion diagnosed as
a result of milder symptoms, such as nocturia, frequency,
and hesitancy, increased. These changes probably would result in the diagnosis of prostate cancers that were detected
following TURP at an earlier stage of disease. Changes in the
SEER coding rules for stage at diagnosis are likely to account
for the increase in the incidence rates for unknown stage
disease in the 1988–1991 period. Since 1988, cancers di-
agnosed by biopsy that were not metastatic have been clas-
sified as unknown stage if no further surgical treatment was
reported. Before 1988 these cancers were staged primarily
as local or regional disease. Misclassification of distant stage
cancers is unlikely to account for the decrease in distant
stage incidence rates. Furthermore, the magnitude of the in-
crease in unknown stage cancers is not large enough to ac-
count for the changes in stage distribution. In addition,
changes in risk factors for prostate cancer may have con-
tributed to the patterns in incidence.

Race and ethnicity are strong determinants of prostate
cancer occurrence; however, the racial and ethnic distrib-
utions of the population in New Mexico were stable over
the study period, and did not account for the trends in in-
cidence rates (17–19, 22, 23). Because the NMTR does not
collect data on risk factors other than demographics, we
were unable to investigate the contribution of saturated fat
and micronutrient intake, occupational exposures, vasec-
tomy frequency, and sexual behavior to prostate cancer in-
cidence and mortality trends (2, 44, 45). Information relat-
ing to these risk factors may not be available from routine med-
ical records, but may be obtained directly from patients as
part of an analytic epidemiological study.

Several factors may underlie the increases in survival,
including more frequent use of radical prostatectomies for
treatment of early stage disease, changes in staging, length-
time bias, and lead-time bias. The increase in relative sur-
vival for local stage disease may reflect an increased diag-
nosis of small, subclinical cancers that contribute little to
mortality and better classification of stage as a result of an-
increased use of prostatectomies (3, 41). The increased pro-
portion of local and regional stage cancer cases treated by
radical prostatectomy resulting in more accurate staging was
accompanied by increases in survival for both local and
regional stage disease, a phenomenon labeled the "Will
Rogers effect." Because 5-year relative survival for local and
regional stage disease increased substantially in all age
groups before the increase in radical prostatectomies, im-
provements in survival can not be entirely explained by
changes in surgical treatment and more accurate staging.
Changes in survival in periods before 1983 may reflect
length-time and lead-time bias. We evaluated length-time
bias by examining changes in histological grade. Although
temporal changes in grade may reflect a number of factors,
the decrease in well differentiated tumors and increase in
moderately differentiated tumors suggest that length-time
bias is an unlikely explanation for the improved survival.
Lead-time bias produced by early detection could explain
the increases in 5-year relative survival for local and regional
stage cancers. We lack complete data on tumor size or other
factors related to lead-time bias to further evaluate the mag-
nitude of effect on survival produced by any lead-time bias.
Increased stage-specific relative survival from improved
treatment might explain a portion of the decrease in mor-
tality; however, treatment with radical prostatectomy has not
been shown to decrease mortality and may increase mor-
tality among elderly men. The decrease in mortality in New
Mexico is unlikely to be explained by improved treatment
from increased use of radical prostatectomy (41). The avail-
able data suggest that the increases in relative survival re-
sulted, in part, from the Will Rogers effect and lead-time bias.

Interpretation of the incidence and mortality trends be-
tween 1969 and 1991 must also consider sources of bias in
the population-based NMTR data. Potential sources of bias
in the NMTR data have been discussed in previous publi-
cations (46, 47). In brief, limitations include the limited va-
lidity of death certificates (48–50), census estimates of New
Mexico’s population, and small numbers of cancers in some
disease stages. Changes in the proportion of cause of deaths
reported as unknown, and in the proportion of deaths from
symptoms, signs, and ill-defined conditions, were small and

<table>
<thead>
<tr>
<th>Stage</th>
<th>Preoperative stage %</th>
<th>Postoperative stage %</th>
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</thead>
<tbody>
<tr>
<td>Local</td>
<td>71.9</td>
<td>33.9</td>
</tr>
<tr>
<td>Regional</td>
<td>28.1</td>
<td>56.2</td>
</tr>
<tr>
<td>Distant</td>
<td>0.0</td>
<td>9.9</td>
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Table 6  Stage reclassification following radical prostatectomy in a New Mexico referral hospital
could not contribute substantially to the prostate cancer mortality trends (data not shown).

The epidemic increase in prostate cancer incidence in New Mexico has been an impetus for increased screening using methods of unproven effectiveness. From 1973 to 1990, all cases detected by screening were found by digital rectal examination, usually as a part of a routine physical examination. It is recognized generally that digital rectal examination is associated with early detection of prostate cancer and is an essential part of any screening program; however, the effectiveness of digital rectal examination as a screening tool has not been established (7, 51). The trends in incidence, mortality, and screening-detected cases suggest that the digital rectal examination may be an effective screening method for secondary prevention of prostate cancer. Recently, the use of PSA for prostate cancer screening has increased. PSA may add to the effectiveness of digital rectal examination in detecting early stage cancers; however, the increase has been too recent to influence mortality rates (32, 52). Continued prostate cancer surveillance and further research are needed to obtain population-based prostate cancer screening data and to assess directly the effect of screening frequency and methods on prostate cancer incidence and mortality rates.

References
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